



August 15, 2018

Michael T. Kleinman
Adj. Professor and Co-Director
Air Pollution Health Effects Laboratory
Department of Medicine
Division of Occupational and Environmental Health
100 Theory STE 100
Irvine, CA 92697-1830

Brian R. Leahy
Director
Department of Pesticide Regulation
1001 I Street, P.O. Box 4015
Sacramento, CA 95812

Dear Director Leahy:

With this letter I am pleased to transmit to you the Scientific Review Panel on Toxic Air Contaminants' Findings on chlorpyrifos (enclosed). The findings were based on the Panel's review of the Department of Pesticide Regulation's (DPR) draft report titled "Evaluation of Chlorpyrifos as a Toxic Air Contaminant" (July 2018), prepared by DPR and reviewed by the Office of Environmental Health Hazard Assessment.

As required by law, the Panel reviewed the scientific data on which the report is based, the scientific procedures and methods used to support the data, and the conclusions and assessments on which the report is based. The Panel also reviewed comments received and responses to those comments. In approving the report, the Panel unanimously concluded that the report, with the revisions requested by the Panel, is based on sound scientific knowledge, and represents a balanced assessment of our current scientific understanding.

Based on this comprehensive and thorough evaluation of the toxicity database on chlorpyrifos, the Panel concluded that chlorpyrifos should be listed as a toxic air contaminant and recommends that you take the necessary regulatory steps to list chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code section 14023.

Please extend to your staff the Panel's and my appreciation and thanks for their efforts to complete this report and for engaging the Panel in lively discussions to respond to questions and concerns. The Panel thanks and commends DPR for a comprehensive and coherent review of the available literature and the synthesis which lead to a risk assessment that is firmly based on the available scientific information to date.

We ask that the Panel's findings and this letter be made part of the final report.

Sincerely,



Michael T. Kleinman, Ph.D.
Chairman
Scientific Review Panel on Toxic Air Contaminants

cc: Scientific Review Panel Members

Lauren Zeise, Ph.D.
Director
Office of Environmental Health Hazard Assessment

Mary D. Nichols
Chairman
Air Resources Board

Jim Behrmann
Liaison, Scientific Review Panel

Enclosure: Findings of the Scientific Review Panel on the Proposed Identification of
Chlorpyrifos as a Toxic Air Contaminant

Findings of the Scientific Review Panel on the Proposed Identification of Chlorpyrifos as a Toxic Air Contaminant as adopted at the Panel's July 30, 2018 Meeting

The Scientific Review Panel on Toxic Air Contaminants (Panel) reviewed the draft document "**Evaluation of Chlorpyrifos as a Toxic Air Contaminant**," prepared by the Department of Pesticide Regulation (DPR) along with findings prepared by the Office of Environmental Health Hazard Assessment (OEHHA) that propose to identify chlorpyrifos as a toxic air contaminant.

In addition, the Panel reviewed DPR's responses to the comments in the OEHHA document, as well as public comments received during DPR's public comment process and DPR's responses to those comments, and public comments submitted to the Panel during its review.

The Panel received a briefing on the initial DPR draft report in a meeting on December 13, 2017, and a full presentation by DPR staff in its January 23, 2018 meeting. The Panel subsequently reviewed revised reports in meetings on March 2, 2018 and June 12, 2018. At its January 23, 2018 meeting and in subsequent meetings, in addition to hearing presentations from DPR and OEHHA staff, the Panel provided recommendations to DPR, most notably that the primary health endpoint should be developmental neurotoxicity (DNT).

As part of its statutory responsibility, the Panel prepared the following findings based on its review of the chlorpyrifos risk characterization, which are submitted to the DPR Director.

The materials as noted above convincingly demonstrate that:

- (1) Chlorpyrifos is a widely used insecticide in California. Chlorpyrifos is an organophosphate compound that inhibits the enzyme acetylcholinesterase (AChE) which is critical for neurological functions.
- (2) Chlorpyrifos exposure is associated with developmental neurotoxicological effects that have been documented in human epidemiology studies and in laboratory animal studies. Developmental neurotoxicity effects have been demonstrated to occur at levels substantially below the level that causes 10% inhibition of red blood cell (RBC) AChE, an endpoint that was used in previous assessments of Chlorpyrifos toxicity.
- (3) Based on a full review of all currently available science, developmental

neurotoxicity is the appropriate regulatory endpoint for Chlorpyrifos to protect health.

- (4) The physical and chemical properties of Chlorpyrifos and the manner in which it is applied are such that its environmental fate includes substantial release into the environment as an airborne contaminant.
- (5) Such airborne release may occur through its routine use.
- (6) Illnesses that may have been caused by exposures to Chlorpyrifos have been documented in DPR's Pesticide Illness Surveillance Program. Bystander exposures have been well documented and evidence is sufficient to indicate that bystander exposures related to the application of Chlorpyrifos to crops are a matter of health concern.
- (7) Although intake of Chlorpyrifos via food and water make significant contributions to the total body burden of the pesticide, this compound meets the criterion for designation as a toxic air contaminant based strictly on consideration of the combined inhalation and dermal exposure of bystanders.
- (8) The estimated bystander exposures to Chlorpyrifos are at levels that cause concern about the associated health risks. DPR regulations state that if the air concentrations of a pesticide are not ten-fold below the reference concentration (RfC) that is considered protective of human health, the pesticide meets the criteria to be listed as a toxic air contaminant (i.e., exposures should be less than 10% of the RfC).

The Scientific Review Panel commends DPR for a comprehensive and coherent review of the available literature and the synthesis which lead to a risk assessment that is firmly based on the available scientific information to date. The Panel notes that the science on organophosphate pesticide exposures is developing and expanding and that the final revision of the document brings the assessments up to the current state of the science.

DPR conducted a comprehensive review of recently available animal studies and focused on the evidence of neurodevelopmental toxicity at low dose levels. Critical Points of Departure (PoDs) were established from animal studies reporting effects at dose levels that were approximately 10-fold lower than those that inhibit RBC AChE. A target MOE of 100 was selected to be protective of human health for the neurodevelopmental endpoint and is comprised of 10x for interspecies sensitivity and 10x for intraspecies variability. The database for developmental neurotoxicity is growing, and as new data become available DPR can further refine this assessment.

The critical NOELs and the reference concentrations are summarized in the Table 23 below, which was excerpted from the Final Report.

In conclusion, DPR evaluated the strengths and uncertainties associated with the use of the available database for deriving critical endpoints for Chlorpyrifos. DPR provided objective approaches for setting regulatory values that are designed to protect sensitive subpopulations from exposure to Chlorpyrifos. Following the recommendation of the Panel, DPR thoroughly evaluated and identified developmental neurotoxicity as the critical endpoint for the Chlorpyrifos risk assessment.

As required by law, the Panel has reviewed the scientific data on which the report is based, the scientific procedures and methods used to support the data, and the conclusions and assessments on which the report is based. The Panel concludes that the report, with the revisions specified by the Panel, is based on sound scientific knowledge, and represents a balanced assessment of our current scientific understanding.

Based on this comprehensive and thorough evaluation of the toxicity database on Chlorpyrifos, the Panel concludes that Chlorpyrifos should be listed as a toxic air contaminant and recommends that the DPR Director initiate regulatory steps to list Chlorpyrifos as a toxic air contaminant pursuant to Food and Agricultural Code section 14023.

I certify that the above is a true and correct copy of the findings adopted by the Scientific Review Panel on Toxic Air Contaminants on July 30, 2018.



Michael Kleinman, Ph.D.
Chairman
Scientific Review Panel on Toxic Air Contaminants

Table 23. Critical NOELs for Developmental Neurotoxicity used for the Risk Characterization of Chlorpyrifos

Route	PoD ^a	RfD ^b or RfC
Uncertainty Factors (UF)		10 inter 10 intra 1 DNT
Acute Oral [mg/kg/day] Infants Children 1-2 Children 6-12 Females 13-49	0.01	0.0001
Acute Dermal [mg/kg/day]# Infants Children 1-2 Children 6-12 Females 13-49	0.104	0.001
Acute Inhalation [mg/m³]# Infants Children 1-2 Children 6-12 Females 13-49	0.405 0.459 0.624 0.862	0.004 0.005 0.006 0.009

^a PoD - Point of Departure (PoD): The critical acute oral PoD for CPF is a NOEL (No-Observed Effect Level) for developmental neurotoxicity in animals based on changes in cognition, motor control and behavior in rats and mice (Lee et al, 2015, Silva et al, 2017, Carr et al, 2017, Gómez-Giménez, 2017, 2018).

^b RfD - Reference Dose (RfD) or Reference Concentration (RfC): RfD and RfC are derived by dividing the appropriate PoD by the product of all uncertainty factors (UF).

Route to route extrapolation:

Dermal: Route specific dermal PoD: oral PoD in animals (mg/kg/day) / dermal absorption in human (9.6% ; Thongsinthusak, 1991).

Inhalation: Route specific inhalation PoD: oral dose mg/kg/day / [Breathing Rate (BR) m³/hr/Body Weight (BW) kg]; Oral PoD=0.01 mg/kg/day; Infants BR=0.188 m³/h BW= 7.6 kg; Children 1-2 yrs BR=0.283 m³/h BW=13 kg; Children 6-12 yrs BR= 0.417 m³/h, BW=26 kg; Females 13-49 yrs BR=0.833 m³/h, BW 71.8 kg (derived from Andrews and Patterson (2000) assuming 24-hr breathing rates of 0.59, 0.52, 0.38 and 0.28 m³/kg/24 hr for infants, children 1-2 yr, children 6-12 yr and females 13-49 yr, respectively.) [See Appendix 4.]